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Low yield of population-based screening for Type 2 diabetes in the Netherlands: the ADDITION Netherlands study

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Janssen PGH, Gorter KJ, Stolk RP and Rutten GEHM. Low yield of population-based screening for Type 2 diabetes in the Netherlands: the ADDITION Netherlands study. *Family Practice* 2007; **24**: 555–561.

Background. About 10 years ago, it was estimated that half of all people with diabetes were unrecognized. Since then, according to the national guidelines, case finding for diabetes in general practice has become common in the Netherlands, resulting in a substantial increase of the prevalence of known diabetes. Nevertheless, the need for population-based screening is advocated, especially by the national federation of diabetes patients.

Objective. To evaluate the efficiency of population-based screening for Type 2 diabetes.

Methods. From 2002 to 2004, we performed a four-step screening procedure [questionnaire, random glucose measurement, fasting glucose measurement and oral glucose tolerance test (OGTT)] and a three-step procedure (without random glucose measurement) in 79 general practices in the southwestern region of the Netherlands.

Results. A total of 56 978 non-diabetic subjects, aged 50–70 years, were asked to complete the questionnaire. Those with a score above threshold underwent further glucose testing. Eventually, 586 participants (1.0%) were diagnosed with Type 2 diabetes (in four-step procedure 285 subjects and in three-step procedure 301). Impaired glucose regulation was assessed in 1011 participants (1.8%). Dropout rate in the screening programme among participants who should undergo an OGTT was 23.4%. The risk score was higher if glucose metabolism was more disturbed.

Conclusion. In the Netherlands, the yield of population-based screening is low. The dropout among high-risk individuals was high. Given the decreasing prevalence of undiagnosed diabetes and the possibility of opportunistic screening on a continuous basis, opportunistic screening for diabetes might be more appropriate than population-based screening. Further research on this topic is needed.

Keywords. Case finding, general practice, opportunistic screening, population-based screening, Type 2 diabetes.

Introduction

Diabetes mellitus is a worldwide rapidly increasing disease.¹ In the Netherlands, the prevalence of diabetes was about 3% in 2003.² Because Type 2 diabetes is often asymptomatic in its early stages, it may remain undiagnosed for many years.³ At the time of diagnosis, however, diabetic complications are frequently present.^{4,5} In this context, screening for diabetes has become a relevant issue. Early detection of diabetes

through screening might be beneficial, although definitive evidence is lacking.⁶ Despite this, screening is recommended by the American Diabetes Association.⁷

Limited information is available regarding the optimal methods for diabetes screening. Therefore, it is disputable how we should screen for diabetes.^{8–11} Many screening programmes combine population-based and targeted (directed at high-risk individuals) strategies in order to enhance the yield.¹² Mostly, a stepped approach is chosen starting with a simple

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risk score to identify high-risk individuals but it is not known how many steps are preferable in a screening programme. The use of a risk score is attractive because it minimizes the number of persons who will attend glucose measurement and therefore reduces costs.¹³ Opportunistic screening or case finding involves screening during routine encounters with the health care system.

Guidelines from the Dutch College of General Practitioners recommend case finding in several well-defined categories of patients at high risk to have undiagnosed Type 2 diabetes (persons older than 45 years with close relatives with Type 2 diabetes, persons with hypertension, an unfavourable lipid profile, obesity or a history of cardiovascular diseases and persons from specific ethnic minorities).¹⁴ The Health Council of the Netherlands recently stated that there is no indication to introduce general screening for diabetes without first demonstrating its effectiveness.¹⁵ To investigate whether early treatment of screen-detected diabetic patients is beneficial, the ADDITION study (Anglo-Danish-Dutch Study of Intensive Treatment in People with Screen Detected Diabetes in Primary Care) has been initiated.¹⁶ In the ADDITION Netherlands study, we performed a four-step and a three-step screening procedure. The aim of the present study was to evaluate the yield of population-based screening for diabetes in the Netherlands. Evaluation took place on the following topics: the percentage of people who showed up for diagnostic testing, the percentage of people diagnosed with diabetes and the percentage of people who did not go through the whole screening procedure. In addition, we compared both screening procedures.

Methods

Patients

All 56 978 patients, aged 50–70 years and not known to have diabetes, from 79 general practices in the southwestern region of the Netherlands were invited to participate in the screening programme. The study was approved by the Medical Ethical Committee of the University Medical Center Utrecht. Participants gave written informed consent.

Practices

Forty-one practices participated in the first screening procedure and 38 in the second. Before the screening programme, the prevalence of known diabetes (in all age groups) in the practices in the four-step and three-step procedures was 3.2% and 3.0%, respectively.

Screening programme

Two stepwise population-based screening procedures were performed. The first screening procedure

consisted of four steps and was carried out from May 2002 to January 2003. The second procedure (from July 2003 to April 2004) consisted of three steps. Assignment to a procedure was done on a geographical basis. Practices closer to the regional laboratory participated in the first screening procedure and practices more distant to the laboratory in the second.

The invitation letter was sent to the patients' home addresses and signed by their own GP. In the Netherlands, practically the entire population is registered with a GP. The letter explained the aim of the study and enclosed an informed consent and a self-completed questionnaire which contained questions about age, gender, body mass index, family history of diabetes, frequent thirst, use of anti-hypertensive medication, shortness of breath, claudication and cycling. Our questionnaire was a slightly modified version of the Symptom Risk Questionnaire used in the Hoorn study^{17,18} and attenuated the impact of age on the score. (In our questionnaire participants in age groups 55–59, 60–64 and 65–69 years scored 1, 2 and 3 points, respectively, whereas in the original version 2, 4 and 6 points were given.) The range of the score was 0–29 points. In the invitation letter it was stated emphatically that further testing was indicated only if the score on the questionnaire was above threshold. However, people with scores under threshold showing up for first glucose measurement were not sent back home. Measurements were performed on special sites in the neighbourhood during and outside ordinary business hours. If participants were unable to come at the given time, they had the opportunity to show up on another day in the same week, even on Saturday morning. If indicated, subsequent testing took place in the week after the first measurement. Participants were classified according to the 1999 World Health Organization (WHO) criteria.¹⁹ Capillary blood glucose values were determined with a HemoCue B-Glucose Analyser based on the glucose-dehydrogenase method.²⁰ Plasma glucose was measured using a peroxidase method.

Four-step screening procedure

The first step of the screening procedure consisted of the questionnaire (Step 1). Participants with a score ≥ 4 points were invited for a random blood glucose (RBG) measurement (Step 2). As a matter of fact, the first procedure was designed not only to screen for Type 2 diabetes but also for impaired glucose tolerance (IGT). Therefore, the cut-off point was 2 points lower than in the second procedure (see three-step screening procedure). If $\text{RBG} \geq 5.5$ mmol/l, a fasting blood glucose (FBG) was measured (Step 3). Participants with an $\text{RBG} \geq 11.1$ mmol/l and $\text{FBG} > 6.0$ mmol/l were diagnosed as diabetic patients. Those with $\text{FBG} > 6.0$ mmol/l but $\text{RBG} < 11.1$ mmol/l were invited for further diagnostic testing by means of a standard 75-g oral glucose tolerance test (OGTT) (Step 4). In

these subjects, diagnosis of diabetes was established if fasting plasma glucose (FPG) or post-load plasma glucose (2-hour PG) in the OGTT was ≥ 7.0 mmol/l or ≥ 11.1 mmol/l, respectively. Subjects who did not achieve a diabetic value in the OGTT were defined as having 'epidemiological diabetes' based on their diabetic FBG. Participants whose FBG concentration was ≥ 5.2 mmol/l and ≤ 6.0 mmol/l also underwent an OGTT. If these subjects had 2-hour PG ≥ 11.1 mmol/l in the OGTT (their first diabetic glucose value), a second OGTT was performed. Subjects with 2-hour PG ≥ 7.8 mmol/l but < 11.1 mmol/l were defined as having IGT. Participants with 2-hour PG < 7.8 were classified as having impaired fasting glucose (IFG) if FBG > 5.6 mmol/l and ≤ 6.0 mmol/l or if FPG ≥ 6.1 and < 7.0 mmol/l. Finally, a letter with the test results was handed over to all participants and the implications were discussed. In addition, participants' GPs were informed.

Three-step screening procedure

Because of costs, in this procedure only capillary blood samples were taken, and glucose measurements outside ordinary business hours and on Saturday were skipped. Participants with a score ≥ 6 points on the questionnaire (Step 1) were invited for FBG measurement (Step 2). RBG measurement was not performed. If FBG > 6.0 mmol/l, a capillary OGTT followed (Step 3). In case of at least one diabetic value in the OGTT, subjects were diagnosed as having diabetes; otherwise, epidemiological diabetes was established. Subjects with FBG ≥ 5.6 mmol/l and ≥ 6.0 were classified as having IFG, they did not undergo an OGTT.

Data analysis

Statistical analyses were performed using SPSS for Windows (version 11.0). To compare characteristics of participants and procedures Student's *t*-test and chi-square test were used. Characteristics of practices in both procedures were analysed with chi-square test. The association between risk score and different glucose tolerance categories was analysed using linear regression. A *P*-value < 0.05 was considered significant.

Results

Of all 56 978 participants, 17 883 showed up to undergo glucose testing. Eventually, 586 subjects (1.0% of the invited people) were diagnosed with Type 2 diabetes. Epidemiological diabetes was assessed in 222 participants (0.4%), impaired glucose regulation (IFG and IGT) in 1011 subjects (1.8%). The dropout rate in the screening programme among participants who should undergo an OGTT was 23.4%. The prevalence of known diabetes in people aged 50–70 years in the practices before and after the screening was 6.1% and 7.0%, respectively.

Four-step screening procedure

Of the 29 251 invited subjects, 11 028 (37.7%) underwent RBG measurement (Fig. 1). FBG was measured in 3243 individuals (11.1%). Eventually, 285 individuals (1.0% of the invited people) were diagnosed with Type 2 diabetes. In addition, we classified 175 subjects (0.6%) with IGT and 218 (0.7%) with IFG. In 126 subjects (0.4%) epidemiological diabetes was established.

After RBG measurement, a total of 323 (9.1%) subjects eligible for FBG measurement did not show up. Of the 747 subjects with FBG ≥ 5.2 mmol/l and ≤ 6.0 mmol/l, 180 (24.1%) did not undergo the OGTT. Among all 462 people who should have an (second) OGTT, 126 subjects (27.3%) dropped out.

A total of 1467 subjects (5.0% of the invited people) attended RBG measurement, although their risk score did not entitle them further testing. Of those, 19 people were classified as having diabetes, 7 as having epidemiological diabetes, 12 as having IGT and 20 as having IFG.

Three-step screening procedure

A total of 27 727 people were invited and 6855 subjects (24.7%) showed up for FBG measurement (Fig. 2). In 397 subjects, an OGTT was performed. In 301 participants (1.1%), diagnosis of diabetes was established. A total of 681 subjects (2.5%) were classified as having IFG. A total of 96 subjects (0.3%) were classified as having epidemiological diabetes. It was not possible to diagnose IGT because an OGTT was performed only in subjects with FBG > 6.0 mmol/l.

Of the 489 subjects who were invited for the OGTT, 92 subjects (18.8%) dropped out. In the second procedure, 1451 subjects (5.2% of the invited people) attended FBG measurement, although their risk score was under threshold. Of those, 43 subjects were classified as having diabetes, 8 as having epidemiological diabetes and 70 as having IFG.

Both screening procedures compared

Characteristics of the two screening procedures are presented in Table 1. The yield of both procedures was similar. In the four-step procedure the yield was 1.0% (screen-detected diabetic patients as a proportion of invited subjects) and that in the three-step procedure 1.1%. When we calculated these percentages after excluding the detected diabetic patients with risk scores under threshold, we found 0.9% in both procedures.

We calculated the mean risk scores (\pm SD) for each diagnostic category. In the four-step procedure, the risk score in those subjects attending the screening with normal glucose tolerance (NGT) was 7.5 (± 4.3). Those with IFG, IGT and epidemiological diabetes scored 8.5 (± 4.9), 8.9 (± 4.5) and 9.8 (± 5.2), respectively. The risk score of diabetic patients was 10.5 ± 5.0 . In the three-step procedure risk scores were as

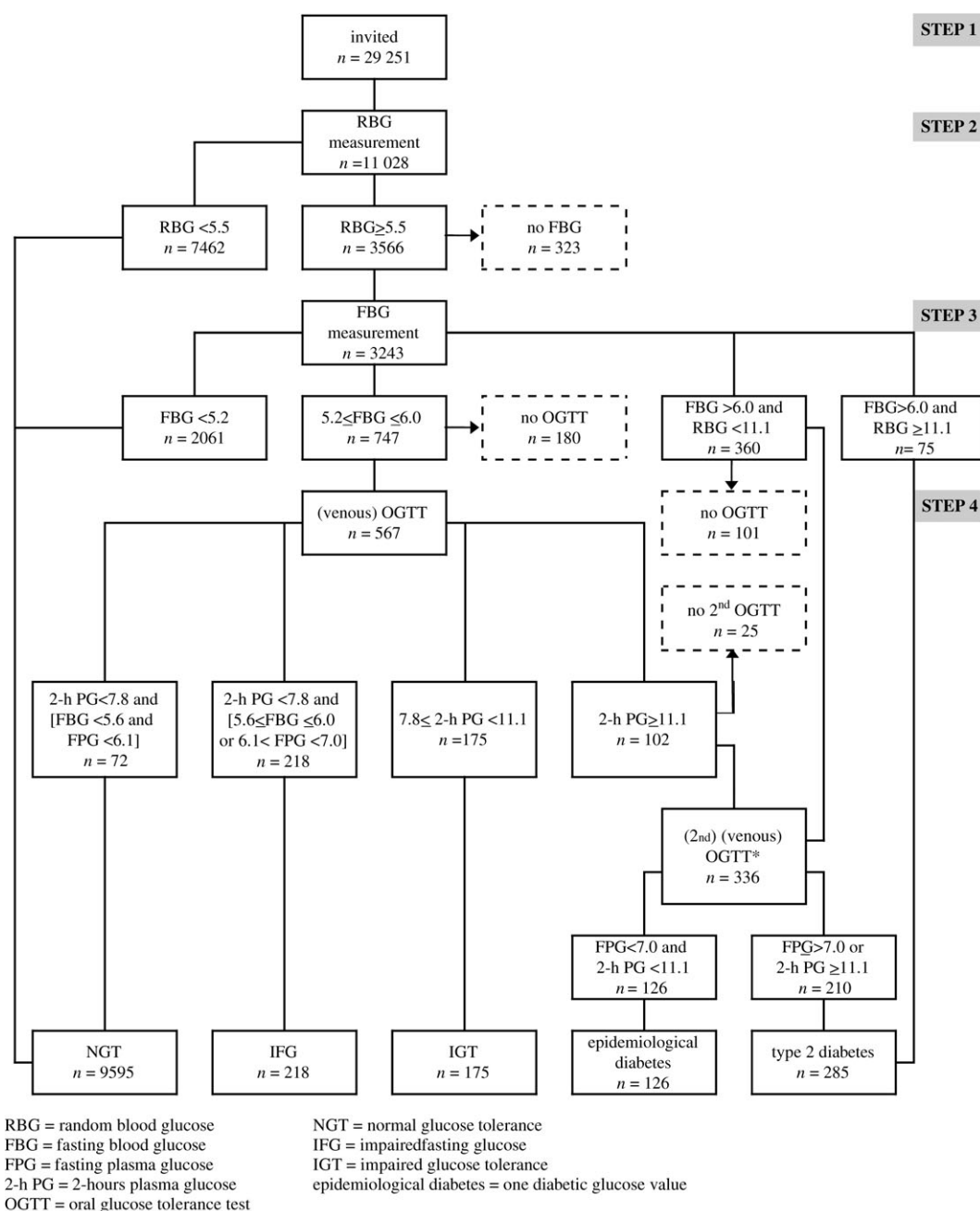


FIGURE 1 Outline of the four-step screening procedure. Between dotted lines: patients who did not show up. Asterisk indicates second OGTT for subjects with 5.2 mmol/l ≤ FBG ≤ 6.0 mmol/l, first OGTT for those with FBG > 6.0 mmol/l and RBG < 11.1 mmol/l

follows: 8.0 (±4.1) (NGT), 9.2 (±4.2) (IGT), 10.0 (±4.2) (epidemiological diabetes) and 10.3 (±4.7) (Type 2 diabetes). In both screening procedures the risk score proved to be higher if glucose metabolism was more disturbed (test for trend: $P < 0.001$).

Comparing the 41 practices in the four-step procedure with the 38 practices in the three-step procedure, we found 22 (53.7%) and 15 practices (39.5%), respectively, to be single-handed ($P = 0.207$).

Of the practices in the four-step procedure, 48.8% was rural, while this percentage in the three-step

procedure was 68.4% ($P = 0.077$). In the four-step procedure, five practices participated with ≥10% patients from ethnic minority groups and 1 practice in the three-step procedure ($P = 0.109$).

Discussion

One-third of the invited persons attended first glucose measurement which is comparable with the findings in the Dutch Hoorn study.¹⁷ Approximately a quarter of

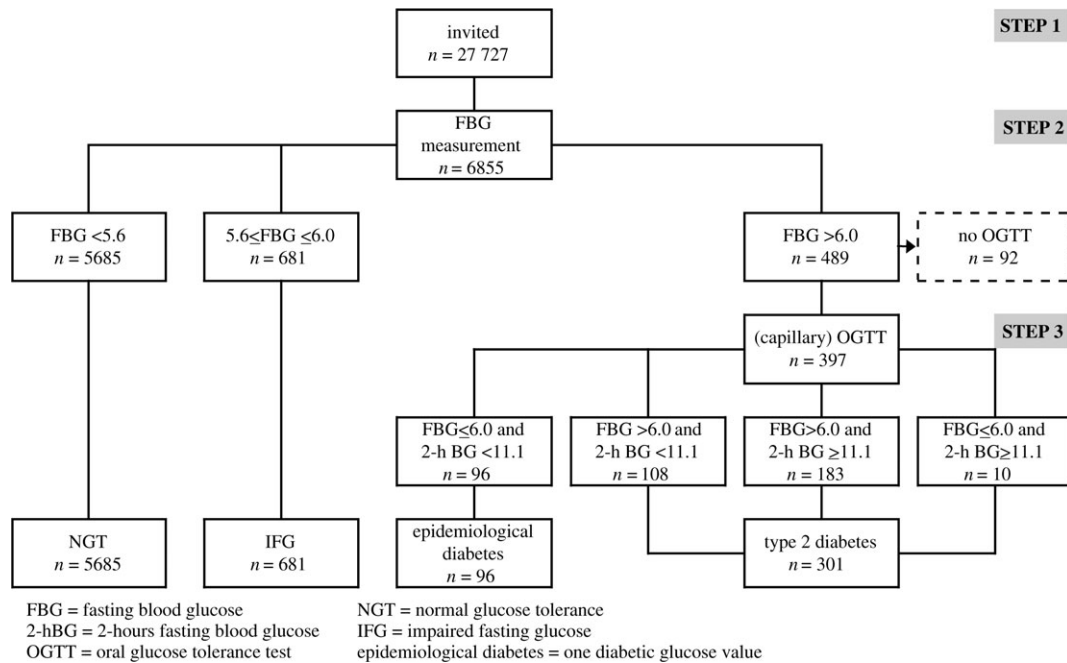


FIGURE 2 Outline of the three-step screening procedure. Between dotted lines: patients who did not show up

TABLE 1 Results of both screening procedures

	Four-step screening procedure	Three-step screening procedure	P-value
Invited (n)	29 251	27 727	
Attendance first glucose measurement (%)	37.7	24.7	— ^a
Gender (male %)	44.7	45.1	0.595
Age (years) (±SD)	59.5 ± 5.4	60.1 ± 5.7	— ^a
Risk score (patients) (±SD)	7.7 ± 4.4	8.2 ± 4.2	— ^a
Glucose measurement			
RBG measurement (n)	11 028	—	
FBG measurement (n)	3243	6855	
OGTT measurement (n)	903	397	
Did not attend OGTT measurement (n)	306	92	
Diagnostic category			
NGT (n)	9595	5685	
IFG (n)	218	681	
IGT (n)	175	—	
Epidemiological diabetes (n)	126	96	
Type 2 diabetes (n)	285	301	
Screen-detected diabetic patients as a proportion of invited subjects (%)	1.0	1.1	0.188
Screen-detected diabetic patients as a proportion of already known diabetic patients (%)	6.8	7.9	0.051

Epidemiological diabetes, one diabetic glucose value.

^aResult of different selection criteria.

the participants, invited for the OGTT, did not show up. The yield of our population-based diabetes-screening programme was low (1.0% of the invited people was

diagnosed with diabetes). In addition, the yields in the four-step and three-step procedures were not significantly different (1.0% and 1.1%, respectively).

Some limitations regarding the comparison of the two screening procedures need to be taken into consideration. Firstly, a considerable number of people who might be at high risk for diabetes did not attend the screening at all. However, since dropout rates were high among high-risk individuals within both screening procedures, it is unlikely that the comparison is distorted. Secondly, it cannot be excluded that temporal trends influenced the yield of screening since both screening procedures were performed successively. But a strong influence is unlikely because in the screening period no new diabetes-screening guidelines were launched. Moreover, characteristics of patients and practices in both procedures were comparable. Thirdly, the comparison between the yields of the two procedures may be distorted because of different methods of diagnosing. In the four-step procedure, all participants underwent plasma glucose measurement as well as capillary blood glucose measurement. In the three-step procedure diagnosis of diabetes was based on only capillary samples. However, the WHO does not set plasma glucose measurement as the gold standard for diagnosis of diabetes and allows the use of capillary samples. Although there is debate on the degree of concordance,²¹ Sandbaek *et al.*²² found both tests to produce equivalent ascertainment of the prevalence of confirmed diabetes. Furthermore, in the four-step procedure some people were diagnosed with diabetes without having an OGTT. There is

a possibility that these differences in used algorithms and methods of diagnosing influenced the yields of screening.

We found an increase of 0.9% in the prevalence of known diabetes after the screening programme. In the Hoorn study (1989–1992) an increase of almost 5% was reported, although the age group was a little different (50–75 years).²³ The yield of the screening programme in the Hoorn study, which was performed from 1998 to 2000 in people aged 50–75 years, was 1.9% (screen-detected diabetic patients as a proportion of invited subjects), which is almost twice as high as the yield of our programme.¹⁷ In the mid-nineties of the last century, it was estimated that about half of all people with diabetes were undiagnosed, but we may conclude that is no longer the case. Following recommendations of the Dutch College of General Practitioners screening for diabetes has become more common in Dutch general practices in the last decade which is reflected by a strong increase of the prevalence of diabetes in the late nineties.² It should be emphasized that the true prevalence of undiagnosed diabetes remains unknown. Nevertheless, we may assume that the low yield of our screening programme was associated with the decreasing prevalence of undiagnosed diabetes.

In Denmark, Christensen *et al.*¹¹ recently found only 0.6% screen-detected diabetic patients (between 40 and 70 years of age), mainly due to a large dropout prior to entry into the screening programme. The authors stated that population-based screening for diabetes is ineffective in general practice. In the English part of the ADDITION study (Cambridge), high-risk individuals for diabetes were initially identified by a simple risk score using data routinely available in general practice.²⁴ In the UK, of the participants who attended first glucose measurement, eventually 2.7% were diagnosed with diabetes. In the ADDITION Netherlands study, this percentage was 3.3%. These findings suggest that the tool used in the UK and the questionnaire in our screening procedure did not perform substantially different.

In our study, the dropout rates within the screening programme were very high among subjects who should undergo an OGTT, demonstrating the difficulties with the OGTT in a screening programme. As non-response frequently is selective, a higher prevalence of undiagnosed diabetes in the group of non-responders is quite conceivable.

Against this background, one could argue that case finding in general practice is possibly more suitable for detecting unknown diabetes than population-based screening. Conducting a screening programme is an expensive and time-consuming process. Case finding, incorporated in daily practice, is lacking these disadvantages. In the Netherlands, necessary conditions for successful case finding are fulfilled: practically the

entire population is registered with a GP and general practices are well organized with respect to daily diabetes care (involvement of practice assistants, practice nurses and diabetes nurses in diabetes care). Additionally, case finding seems more applicable than other screening strategies in fulfilling the criterion that screening should be a continuous process.²⁵ Moreover, we found that glucose intolerance is associated with the height of the risk score: the higher the score, the poorer the glycaemic control. This reveals another possible advantage of case finding: it may offer the possibility of detecting persons with impaired glucose regulation who have already increased risk for cardiovascular diseases.²⁶ The considerable number of detected subjects with impaired glucose regulation impels to a proactive approach of health care providers in order to reduce their cardiovascular risk.²⁷

It should be noted that Dutch GPs are not accustomed to perform the OGTT in daily practice. Consequently, diagnosis of diabetes will be missed in those who have only diabetic post-load glucose values. However, this is likely a relatively small group. In our four-step screening programme, of the 747 persons with non-diabetic fasting glucose values who were invited to undergo the OGTT, eventually only 35 were diagnosed with diabetes (although it is assumable that this small number partially can be explained by the high proportion of subjects who did not attend the OGTT).

In summary, the yield of population-based screening for diabetes in the Netherlands was less than expected. Given the decreasing prevalence of undiagnosed diabetes and the availability of well-organized general practices regarding diabetes care in the Netherlands, case finding might be more appropriate for detecting unrecognized diabetic patients than population-based screening.

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Declaration

Ethical approval: None.

Conflicts of interests: None declared.

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